Remarks

The above Amendments and these Remarks are in reply to the Office Action mailed July 2, 2003.

Claims 1 - 29 were pending in the Application prior to the outstanding Office Action. Applicants have added new claims 95 - 107, Thus, claims 1-29 and 95-107 are in this application.

Applicants have amended the first paragraph of the specification to provided updated information on the claim for priority. Applicants have amended claim 1 and have added new claims 95 - 107. Applicants submit that the amendment to claim 1 merely makes explicit that which was implicit in the original claim., namely that a "multivalent cation" is a "multivalent, monoatomic cation," and that therefore, the amendment is not a narrowing amendment.

I. Rejections Under 35 U.S.C. §103 Over Tapolsky and Jacob

Claims 1-29 stand rejected under 35 U.S.C. §103(a) as obvious over the combination of Tapolsky (U.S. Patent No: 5,800,832; "Tapolsky") and Jacob (U.S. Patent No: 5,985,312; "Jacob").

According to the Examiner, "Tapolsky teaches a polymeric composition comprising carboxypolysaccharides. . . and polyalkylene oxides. . . Tapolsky also teaches the addition of antithrombogenic agents. . . however, Tapolsky does not teach the addition of a multivalent/divalent cation." Office Action, page 4, second paragraph.

Furthermore, the Examiner stated: "Jacob teaches that the addition of multivalent metal compounds, i.e., Ca^{2+}, Mg^{2+}, $Fe^{2+,3+}$, Al^{3+} to polymer compositions containing polyacids and polyalkylene oxides improves the bioadhesive properties of these compositions (col. 5, line 57 - col 6, line 62) which adequately bridges the nexus between the prior art and the invention as claimed."

Applicants reiterate all previous arguments and incorporate them herein fully by reference. In particular, Applicants submit that the above recitation from Jacob is nonsensical, in that the recited species (Ca^{2+} etc.) cannot be "compounds" as the term is understood in the chemical arts.

In particular, Applicants respectfully submit that Jacob does not teach the use of "multivalent monoatomic cations" as in amended Claim 1, but rather discloses the use of "metal compounds." Applicants note that the term "metal compounds" as disclosed by Jacob refers mostly to "[m]etal compounds which enhance the bioadhesive properties of a polymer, preferably are water-insoluble

metal compounds, such as water-insoluble metal oxides and hydroxides. . . ." Column 3, lines 47 - 49. Moreover, in many cases in Jacob, the term "metal compound" is used in the phrase "water-insoluble metal compounds" (col. 5, line 9), "metal compound . . as a dispersion of a water-insoluble metal oxide" (col. 5, lines 24-25), "water insoluble metal compound" (col 4, lines 42-43). Additionally, "a water insoluble metal compound is defined as a metal compound with little or no solubility in water, for example, less than about 0.0 - 0.9 mg/ml." Col. 4, lines 43-46.

Applicants respectfully traverse the Examiner's comment "Applicant's recitation of a dictionary definition of metal compounds is moot given that one of skill in the art need only reference the teachings disclosed in Jacob for the definition." As described more fully below, Jacob's "teaching" is at best, ambiguous, in that for example, Ca^{2+} cannot be a "metal compound" but rather is a completely ionized, monoatomic metal ion. Thus, because of the ambiguous teaching of Jacob, a person of ordinary skill would not know what is meant by the term "metal compound," and reference to other information is necessary (e.g., dictionary definitions).

Accordingly, the McGraw Hill Dictionary, page 425, defines a "compound" is defined as "[a] substance whose molecules consist of **unlike atoms** and whose constituents cannot be separated by physical means. Also known as a chemical compound." Emphasis added. Applicant notes that the term "unlike atoms" is in the plural.

Therefore, according to the above definition, Jacob's "metal compound" would be made of at least two unlike atoms. All of the examples of "metal compounds" disclosed in Jacob are made of unlike atoms, and includes metal oxides, metal hydroxides and the like. However, Applicants can find no disclosure of any "multivalent monoatomic cation" in Jacob. At best, Jacob refers to "**partially ionized** metal compounds" (col 6, lines 41 - 42; emphasis added), but Applicants can find no teaching, disclosure or suggestion of a composition comprising a "multivalent cation."

Further, Applicants note that the terms Ca^{+2}, Mg^{2+}, Mn^{2+}, Co^{2+}, Al^{3+}, Fe^{3+} and the like refer to **completely ionized** species, i.e., "monoatomic" cations. They therefore cannot be part of a "partially ionized metal compound" in which the metal is necessarily incompletely ionized. If a valence electron is used to form a bond between a metal atom (e.g., calcium atom) and an oxygen atom to form a "metal compound" (e.g, an oxide), that valence bonding electron cannot simultaneously be lost to form a completely ionized metal atom. Thus, for example, calcium oxide (CaO) were to be ionized, the calcium atom would necessarily have less than two positive charges because one of the two valence

electrons must shared with the oxygen atom to keep the compound intact. Thus, to shed the second of the two electrons (i.e., the bonding electron), the calcium oxide compound would necessarily fall apart and could not be thereafter be considered to be a "compound." Applicants therefore respectfully submit that the use of the term "partially ionized metal compound" of Jacob therefore cannot refer to a "monoatomic multivalent cation" of Claim 1 or to Ca^{+2}, Mg^{2+}, Mn^{2+}, Co^{2+}, Al^{3+}, Fe^{3+} or other completely ionozed atom.

In response to the Examiner's comments regarding Applicants' prior arguments referred to on page 3 of the Office Action, Applicants submit that the claimed compositions and those of Jacob are not "analogous." A person of ordinary skill in the chemistry arts would appreciate that the terms "divalent" and "trivalent" could refer to the total number of valence electrons present. As such, calcium atoms typically have two valence electrons and iron atoms typically have three valence electrons. As noted above, the total number of valence electrons in a compound is necessarily distributed between bonding electrons and non-bonding (or "ionizable") electrons. In a compound, bonding electrons cannot be dissociated, and therefore, that any "metal compound" including calcium cannot under normal conditions have two net positive charges. Thus, Applicants' use of the terms Ca^{+2}, Mg^{2+}, Mn^{2+}, Co^{2+}, Al^{3+}, Fe^{3+} and the like, cannot include "partially ionized metal compounds" because, by definition, the above terms can mean only completely dissociated cationic species, which are therefore "monoatomic." Thus, "metal compositions" of Jacob are not "analogous valence metal compositions" as indicated by the Examiner.

Further, as the Examiner aptly pointed out, Jacob (col 5, line 28) teaches: "[f]or example, in one embodiment, **water-insoluble metal oxide particles** are incorporated into a polymer defining or coating a microsphere or microcapsule used for drug delivery." Thus, Jacob teaches a different composition than those claimed, and reliance on an intended use of the composition, even if similar, is insufficient to define a composition in a fashion inconsistent with the plain meaning of the words defining the composition itself. Jacob states an aim to provide:

> enhanced binding of the polymers incorporating a metal compound is due to the presence of **partially ionized metal compounds**, such as divalent or trivalent cations, on the surface of the polymer which interact, for example, via an ionic binding attraction with negatively charged glycosubstances such as sialic acid and L-fucose groups on the mucosal membrane surface. **Multivalent ions such as divalent or trivalent cations in the metal compounds generally have the**

> **strongest affinity for the negatively-charged mucin chains."** Column 6, lines 40-49; emphasis added.

In addition to the term "divalent or trivalent cations in the metal compounds" being nonsensical when applied to calcium, Applicants submit that the focus in Jacob is with the attraction between the metal compound and tissues, where a "**partially ionized** metal compound" of a polymer would be bound with the tissue.

In contrast, the role of "monoatomic multivalent cations" in Applicants' gels is different. As indicated in the specification at page 25, lines 17 - 26:

> Although the exact mechanism of ionic cross-linking of polyacid/polyether association complex formation is not completely known, one theory is that ionic bonding or association occurs between the acid residues of the polyacid and the ether oxygen atoms of the polyether. According to this theory, divalent ions such as calcium (Ca^{2+}), cobalt (Co^{2+}), magnesium (Mg^{2+}), manganese (Mn^{2+}) and trivalent ions such as iron (Fe^{3+}) and aluminum (Al^{3+}) can lie between the acidic residues of the poly acid and the ether oxygen atoms of the polyether and can be attracted to valence electrons with the acid and oxygen atoms, thereby forming an ionic bond.

Therefore, Applicants use of "multivalent cations" of the instant claims refers to the **internal bonding of the gel components with each other**, to provide control over physical properties of the gel, such as viscosity, and not between the metal compound in the "polymer which interact, ... with negatively charged glycosubstances... on the mucosal membrane surface" as described by Jacob.

Thus, Jacob's disclosure pertains to increasing the adhesion of polymers to tissues using metal compounds, whereas Applicants' invention is directed use of "multivalent monoatomic cations" to provide gels having desirable properties, including viscoelastic properties.

Applicants respectfully submit that Jacob neither teaches nor suggests a "multivalent monoatomic cation" as in Applicants claims. Further, Applicants can find no teaching or suggestion in Tapolsky of the use of "a multivalent cation", and thus, Tapolsky cannot make up for the lack of such teaching or suggestion in Jacob. Because there is no teaching or suggestion in Jacob of the use of a "multivalent monovalent cation," Applicants submit that the combination of Jacob and Topolsky together would not result in the Applicants' invention as claimed in claim 1. Because all of the other rejected claims depend directly or ultimately from claim 1, or include the limitation to "multivalent

monoatomic cation," Applicants submit that none of the claims are rendered obvious by Tapolsky and Jacob, and urge the Examiner to reconsider the rejections and find the claims allowable.

Finally, Applicants have added new claims 95-104, which depend ultimately from claim 1. Support for those claims can be found in the specification at least at page 28, lines 23 - 28. THose dependent claims therefore include all the limitations of claim 1, and therefore should be allowable. Although Claim 105 is drafted in independent form, it includes the same limitations of claim 1 including "multivalent monoatomic cation," and therefore should be allowable.

III. Conclusion

Applicants conclude from the above discussion that none of the cited prior art (1) discloses all the elements of the instant claims, or (2) when taken either separately or together teaches or suggests all elements of the claims. Thus, Applicants respectfully submit that the combination of Tapolsky and Jacob, together or separately, cannot render the instant claims obvious to a person of ordinary skill without undue experimentation with a reasonable likelihood of success. Therefore, Applicants believe that no prima facie case for obviousness has been made, and urge the Examiner to reconsider the rejections and find the claims allowable.

In light of the above, it is respectfully submitted that all of the claims now pending in the subject patent application should be allowable, and a Notice of Allowance is requested. The Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting issuance of a patent.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 06-1325 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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